condition in humans would produce the same result. And if it did produce the same artificial result, one would have the additional problem that EAU in humans has no exact disease correlate. Therefore, the two Dick articles do not disclose the claimed invention for at least 2 reasons: 1) it is done with rats, whose biochemistry differs in many important respects with the human; and 2) it is a rat model of EAU, which has no exact disease correlate in rats and certainly none in humans.

The reference to Sippy studied RPE cells, which were isolated from fetal eyes and then cultured in artificial medium. In this situation, the scientists assumed the cultures were not contaminated by other cells. This experimental situation is, of course, entirely artificial. Not only is it ex vivo, it is also entirely an artificial model using animal and other elements which are not human. For example, Dulbecco's modified Eagle's medium is supplemented with glutamine, penicillin, streptomycin and, most importantly, fetal bovine serum. In addition to the bovine and bacterial elements, the tissue being studied is cultured human fetal tissue which, of course, cannot be used to exactly predict the behavior of in vivo post-fetal human tissue. In the next part of the study, donor adult eyes were obtained from aged (ages 71-93) human eyes after death of the patients. The patients' pre-morbid condition was not specified, except to say that they were not "clinically immunosuppressed" and "had not been on anti-inflammatory medications."

The author's own conclusion in this article (page 314) is that "the potential significance of these soluble TNFRs in ocular disease remains unclear." The author further

states, on page 315, the following: "It remains unclear, however, whether soluble p55 could diffuse from the RPE through the sensory retina to the vitreous cavity." They go on to discuss the fact that soluble TNRFs may have contradictory effects, in some cases acting as a TNF antagonist and in others as a TNF agonist.

Sippy does not disclose or teach the use of the specific TNF antagonist medications claimed in the present application. The experimental model of Sippy, et al has limitations because of its use of bovine and bacterial products, artificial cell culture, and post-mortem eye extracts from deceased human donors whose clinical condition was not fully characterized.

We therefore respectfully submit that although these articles are certainly of interest to the scientific community, they do not constitute prior art that would negate the present patent claims in consideration.

For the same reasons, we respectfully submit that the above three articles have no relation to the issued patent of Sadun.

We therefore proceed to analyze the patent of Sadun with regard to its relation to the submitted patent claims.

First, there is no mention of the use of soluble TNF receptors or a fusion protein in the Sadun patent. Etanercept, as mentioned in the submitted patent claim, is a fusion protein containing two soluble TNF receptors attached to an Fc fragment of an immunoglobulin molecule. It is not a TNF antibody, nor is it an antisense DNA molecule. Etanercept and

pentoxifylline are completely different agents, and have different structures and will function differently. The submitted claims recite very specific TNF antagonists that have structures different from pentoxifylline. Thus, the Sadun patent does not teach that the TNF antagonists claimed by applicant will be effective in treating the disorders claimed.

Respectfully submitted,

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By Judith M. Grania